RESEARCH ETHICS

# Enhancing the ethical conduct of genetic research: investigating views of parents on including their healthy children in a study on mild hearing loss

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Clinical genetic research is often regarded as more ethically problematic than other forms of research, and in some countries is subject to specific regulation, requiring researchers to follow specialised guidelines. In this paper, an approach to enhancing the ethical conduct of genetic research is proposed, which is believed to be more effective than simply attempting to follow general guidelines. The potential concerns, likely areas of misunderstanding and negative reactions of the participant group are systematically investigated before starting a study on genetics. This would constitute, in effect, an ethical pilot study, similar to a feasibility pilot study to test equipment, procedures and logistics. The findings of the ethical pilot study would be used to help in designing ethically important aspects of research protocol, such as recruitment procedures, written and other information for potential participants, informed consent processes and reporting of results including ambiguous or uncertain results.

Clinical genetic research is often regarded as more ethically problematic than other forms of research, and in some countries is subject to specific regulation.[1] Problematic issues include whether and how to report results, especially if their relevance is uncertain;[2] the potential risks (including potential discrimination in employment or insurance because of having a genetic test);[3] how to appropriately inform participants of these risks;[4] and the potential personal implications of genetic knowledge, including the implications for family members, effects on family relationships, and accidental disclosure of non-paternity.[5] Given these potential ethical problems, it is clearly important to find a way to conduct genetic studies in an ethically sensitive manner. How to do this, however, is not so clear. Although some attempts have been made to set out quite detailed guidelines for the conduct of genetic research (eg, in Australia[6] and Canada[7]), these guidelines are necessarily still quite general, and arguably not all equally relevant to the vast range of different types of genetic research. In this paper, we put forward a different approach to enhancing the ethical conduct of research in genetic testing, which we believe will be more effective than simply attempting to follow general guidelines.

The approach we recommend is to systematically investigate the potential concerns, likely areas of misunderstanding and possible negative reactions of the participant group before starting a genetic study. This would involve, in effect, conducting an ethical pilot study, in much the same way as a pilot study to test equipment, procedures and logistics is conducted. The findings of the ethical pilot study would then be used to help in designing ethically relevant aspects of the research protocol, such as recruitment procedures, written and other information for potential participants, informed consent processes, follow-up support for participants, protocols for the storage of genetic information and the reporting of individual results, including ambiguous or uncertain results.

In this paper, we demonstrate how this approach would work by describing just such an ethical pilot study, and discussing the use of its results in the design of the main study. The main study in question was an investigation of the underlying genetic causes of slight or mild sensorineural hearing loss in children. Given recent advances in knowledge of the genetics of moderate–profound nonsyndromic hereditary hearing impairment,[8 9] we aimed to find out whether, how much or in what ways the ''deafness genes'' identified already (in this case connexin 26 mutations) contribute to slight or mild hearing impairment. The main study also aimed at assessing the effect of slight or mild hearing loss on a child's language, learning and quality of life. The rationale for the study was that improved understanding of the contribution of the deafness genes to slight or mild hearing loss will enable more accurate counselling of those who are identified with mutations in the deafness gene in either the homozygotic or the heterozygotic state, whether their hearing loss is slight or profound.

We suggest that this approach of doing an ethical pilot study is applicable to any study involving genetic testing, regardless of the nature of the condition and participant group. The qualitative method that we describe can be used in any setting, with interview questions along the same general lines, but using the particular features of the proposed genetic research project where appropriate. It would also be possible and valuable to use approaches from participatory action research methods, which are particularly well suited to projects designed to enhance the

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**Table 1** Characteristics of the sample

| Child | |
|---|---|
| Year level (n, %) | |
| Grade 1 | 8 (47.1) |
| Grade 5 | 9 (52.9) |
| Hearing result (n, % OME) | 9 (52.9) |
| Parent (n, %) | |
| Sex: female | 13 (76.5) |
| Ancestry: Australian | 10 (58.8) |
| High education level* | 13 (76.5) |

OME, otitis media with effusion.
*High education level is defined as a parent having a tertiary qualification.

understanding or knowledge of participants, and to provide health professionals with some insight into the participants' ways of seeing the world. We will show later in the paper that the potential uses of the findings from an ethics pilot study would likewise be similar in any setting.

## THE ETHICAL PILOT STUDY

### Methods and participants

The study involved individual interviews with 17 parents of primary schoolchildren. Parents were recruited through two government primary schools in a mid-socioeconomic status suburb of Melbourne, Australia, when they consented to their child's participation in a pilot hearing test for the main study. Purposive sampling ensured a spread of participants across parental education, sex, migrant status, child's grade level and child otitis media with effusion (OME or glue ear, table 1). This qualitative study, based on grounded theory, was designed on the rationale that open-ended questioning is the best way to establish initial knowledge of an under-investigated phenomenon. The Royal Children's Hospital Ethics in Human Research Committee (EHRC 22056A) approved the study.

Parents were interviewed individually using a semistructured interview guide that covered their views on genetic testing in general and their attitudes and possible concerns on their children participating in a genetic research study on hearing loss (details of which were explained). The interviews were conducted at a location convenient for participants, predominantly at their home, the school their child attended or at their place of work. On completion of the interview, participants were given a list of items, which contained information we were considering whether to include in the written information to be given to participants in the main study (table 2). The items were based partly on the information that the national research ethics guidelines in Australia require participants in genetic research to be given.[6] Participants read each guideline aloud and were asked the following questions: ''Does it seem relevant/important to you? What is your response to it? Is it helpful/reassuring or worrying in some way? Do you think it is important to tell people this piece of information?'' Interviews were taped and transcribed. To ensure reliability, data were subjected to independent content and thematic analysis by three researchers. Thematic analysis proceeded by first coding the important elements of each participant's responses to the interview questions and then identifying common themes across interviews. Finally, connections and disjunctions between common themes were analysed.

Names of participants and other identifying information were removed from transcripts to protect confidentiality, and participants are referred to here only by number. The source of quotes is given as a page and line number from the transcripts. So, for example, 2.4.17 means interview 2, page 4, line 17.

## RESULTS

The study showed that parents were largely unfamiliar with genetic testing of any sort. None of the parents reported having had a genetic test themselves, and only three of them knew of anyone who had. When asked what genetic conditions they knew of, the responses (table 3) showed a surprising lack of familiarity with common inherited genetic conditions. We observed a concentration on cancer, which, although genetic, is in most cases not inherited. They had more understanding of how genetic testing would be carried out, with most aware that some form of tissue sample would be taken. Most commonly, they pictured this as a blood test.

From their responses to questions about what they would want to know about the study, clearly, the focus of parents' concern was on the immediate effects on the child participating in the study, not on the specifically genetic

**Table 2** Items of information

1. The sample for genetic testing will be taken by brushing inside your child's cheek, not by taking blood.
2. Your child's genetic test information (if he or she has a hearing loss) will not be given to you (the parents) until about 18 months after the genetic test is done. If your child does not have a hearing loss, we will not tell you your child's results, as there would be nothing informative in this for you.
3. We don't know yet whether the study will provide the sort of information that could be useful to the future health of your child. This study will not produce a new treatment for hearing loss for your child, but might help contribute to better management and treatment in the future.
4. *Genetic information about your child has implications for other family members—they may have the same genes as your child because they are related.
5. Later in this study, we may approach you again, and ask you (the parents or other family members) to consider having a genetic test as part of the study. Note that you do not have to agree to that now—you can make a choice later.
6. Genetic information obtained from the children will be kept in a password-protected file on the Murdoch Children's Research Institute computer network.
7. Genetic information about your child will be made available only to you, the parents or guardians of the child. The only other people who will have access to the results of the genetic tests with identifying personal details will be the researchers named above and their research assistants.
8. *People who have had a genetic test may have to reveal this to an insurance company, and may have difficulty getting some types of insurance or have their premiums altered as a result. Note that this does not apply to standard private health insurance.
9. *Genetic testing has the potential to reveal non-paternity or non-maternity information, if a child's parents are also tested.
10. Your child's genetic material will be stored in a laboratory at the Murdoch Children's Research Institute. It is possible to use genetic material for purposes other than this study, but to do so requires your consent (unless required by law).

*Required by the Australian guidelines.

**Table 3** Knowledge of genetics

| | | | | |
|---|---|---|---|---|
| Conditions perceived to be genetic (n) | Cystic fibrosis | 3 | Asthma | 1 |
| | Cancer | 3 | Bowel cancer | 1 |
| | Breast cancer | 3 | Heart problem | 1 |
| | Workplace injuries | 1 | Down's syndrome | 1 |
| | Juvenile diabetes | 1 | | |
| Perceptions of what genetic testing is (n) | Blood test | 7 | Amnio[centesis] | 1 |
| | ''Sample'' | 2 | Not a blood test | 1 |
| | Invasive procedure | 2 | Lab test | 1 |
| | Painful procedure | 2 | Swab | 1 |
| | Bone marrow | 2 | Injection | 1 |
| | Take family history | 2 | Cell test | 1 |
| | DNA (whatever genes are?) | 1 | Hair sample | 1 |

aspects of the study. They wanted to know if the procedure would be painful, whether the classroom routine would be disrupted, whether the child would be singled out as different and so on.

> I would probably, as a parent, be particularly interested in invasive procedures, particularly blood taking and things like that, I think that that is what most parents are probably most concerned about. (8.42.29)
> Oh yeah, and the risk side for the child is there, what sort of testing is done and how does it impact on your child and, um, keeping the child informed about what it's supposed to do …. (5.27.1–2)

The next major concern, often occurring in the same breath, was about privacy and who would have access to the child's information.

> How will it affect the child, and what the privacy aspect of it is and how it will be used and what the specific tests are … yeah … is the child going to be injured or you know is there a risk there. I suppose the biggest thing is the privacy element and the risk element for the child. (5.26.45)
> And I'd want to be assured that it would remain private, that it would be anonymous, if it was used in a study or whatever, and that it was just confidential, that's all. (17.74.30)

Concerns on privacy and access may be relevant to any sort of research, but some of the parents' comments indicated that these concerns were heightened because the study was about genetics:

> … a bit of concern as far as people having this all documented—Big Brother is watching you. (3.14.12)
> A whole lot of information about how it's used, about how and where it's kept, that type of information more than just taking it for one issue, you know because it could be kept forever, and I do not want that. I do not want my child's DNA kept anywhere that can be used any other time. (2.10.16)

Despite these general concerns about who would have access to the children's DNA or genetic information, parents were not specifically aware of the possible insurance implications of genetic testing. Once informed (by reading the list of information items at the end of the interview), most people regarded it as very important, often seeing it as a specific example of what they had said earlier about privacy.

> That's where I was saying about who is getting access to it, privacy … I do not want any of these results—that is a big concern because I do not want any of this, to have any of it, on my child's insurance and privacy and these things. (2.11.31)
> Oh yeah, I hadn't thought about that … so yeah it's very important, and I reckon it could sway you as to whether you then decided to participate. (13.65.4)

One participant stated very definitely that she would not allow her child to participate for that reason alone (2.11.75). Others felt that although it was important to make potential participants aware of the issue, it was probably not an important consideration in this case, given that the study involved only children and hearing.

> It's probably raising a … creating a panic button that doesn't need to be there, I imagine, for hearing. (14.68.37)

The question of receiving individual results proved to be important to parents. One parent was very definite: ''I wouldn't do it unless I was going to be given an outcome'' (16.73.7). Another put it somewhat more mildly: ''I would just be interested on an intellectual level to know what the results are across the board, but I also think any parent would be interested to know what health results their kids have'' (8.42.51). Another parent commented that if the test showed that something was wrong with her child that would allow her to ''take this further'', going on to explain that if something was found to be medically wrong with her child, they could follow this up with further testing (10.46.38).

Few were concerned that the results may be inconclusive or not immediately available, provided that this was disclosed at the outset. ''Waiting eighteen months isn't important—I think it is important to know that [there will be a delay]'' (13.64.29), said a parent. Another commented that ''If you are going to reveal a result to people, it would be useful to people to know that the result might be imprecise'' (7.39.38).

For some parents, however, an inconclusive result would be disappointing or would provoke anxiety, and they anticipated feeling that they should try to find out more: ''I would investigate further—parents should'' (6.34.44).

The issue of non-paternity (see table 2, item 9) was not particularly important to participants, although it did seem to make them a little uncomfortable (most laughed when reading it out on the list of information items). Although they generally believed that people should be told of this possibility, they thought it would not deter them from participating.

Overall, parents were quite positive about their child participating in the study as described to them. Their reasons fell into three main categories: the desire to help others, believing that it would help their own child and the desire to contribute to scientific knowledge. One parent succinctly identified all three as reasons why she would agree to her child participating:

> … for the general health of my children and once revealed being able to deal with that result effectively. The benefit to research in general and also to other children. (6.34.52)

Others tended to focus more on one particular reason:

> … so on an individual level it would make perfect sense … particularly if there was a genetic test already and I guess you are contributing say, if John [pseudonym] was tested,

you are contributing to the possibility in the future … people might be assessed at birth or you know even before birth or whatever and measures taken that might help …. (7.38.27)

… simply as a contribution to public health I guess. (14.67.25)

I think that it is good to know if it is something that can be fixed. Especially it is good to know so that he knows for his family or children or whatever, do you know what I mean? (11.50.48)

… for the general health of my children. (6.34.53)

… to find out why he seems to having these problems and his sister isn't. (16.73.21)

More for the research purposes of it, for future … um … generations and use in the medical field. (5.27.75)

In general, parents did not see any strong reasons not to participate. The things that were most important to them (the effects on the child of taking the tissue sample and the privacy of the sample and related information) were dealt with to their satisfaction in the description of the main study that was given to them.

## SIGNIFICANCE OF RESULTS AND USEFULNESS FOR MAIN STUDY DESIGN

One important outcome of this ethical pilot study was that some parents clearly thought that the main study would produce information that was directly relevant to their child's health, and hence that participation would benefit the child. This was evident from one of the reasons parents gave for participating: that it would help their child's hearing or explain the cause of a hearing problem. It was also evident in some parents' reaction to the possibility that they would not get a result for their child, or that it would be inconclusive—they wanted to know their child's result because it would have a bearing on the child's health and they would need to investigate further if it were inconclusive. These views were expressed despite the parents clearly being told that the main study would not necessarily produce useful or meaningful information, and would not produce a new treatment for hearing loss.

The phenomenon of research participants expecting direct benefits when this has explicitly not been offered or guaranteed in the participant information is well known and is widely discussed in the literature as ''therapeutic misconception''.[8] Therapeutic misconception has been documented in adult research participants[9] and also in parents consenting on behalf of child participants.[10] It is usually associated with clinical trials, in which the participants are patients, and the researcher is often their clinician as well.[9 11–13] In our pilot study, the situation was somewhat different, as the children were not currently patients (only half had a history of mild hearing loss due to otitis media with effusion, but this is easily treated as soon as detected) and the research was not being conducted by the children's clinicians. Therapeutic misconception was therefore less easily predicted in this context. The source of the therapeutic misconception in this case appeared to have been the parents' assumptions that meaningful and useful personal genetic information would be disclosed by the study, even though they were told not to expect this.

This is an important issue because it affects the ethical validity of informed consent by parents in the main study. If they consent to the genetic study on the basis of benefits to their child outweighing the risks to their child, then this is not an informed consent, as there will be, in all probability, no benefits to the child from the information produced at the end of the study. Once recognised, steps can be taken to counteract this sort of problem. Obviously, more emphasis needs to be placed on the lack of direct benefits to the child. The plan to report individual results may be misleading the parents into believing that the results will be clinically relevant; this may be countered by explaining more clearly the actual rationale for reporting individual results.

Many other aspects of the findings from the ethical pilot study were relevant to the written information given to parents for the main study. For example, the generally low level of knowledge about genetics suggested the need for care in explaining the genetic aspects of the study. Additionally, the concern about the immediate effects on the child, and the common belief that genetic tests mean taking blood, highlighted the importance of explaining the cheek swab method of collecting a tissue sample, emphasising that it is a non-painful, non-invasive procedure.

The results from the ethical pilot study described here were subsequently used, as planned, to inform a nested case–control study on children with slight or mild hearing impairment (cases) and children with normal hearing (controls); these two groups were selected from a larger population-based survey (the Hearing In Schools Study). These data helped shape the supporting information offered at the time of seeking informed consent, and planning and managing the process of offering individual genetic results. As the participants clearly expressed that, as parents, they wanted to know their child's results, it was decided that letters would be sent to parents of all children, cases and controls, on completion of the study. For children in whom a genetic change was found, care was taken to explain in the letter that this finding had no known implications for the child's hearing or any other aspect of their health, given the tendency for therapeutic misconception as described earlier in this paper. If parents of participants were still concerned or still believed that they needed to take some action, they were also offered the option of meeting a medical geneticist to discuss their child's results.

## CONCLUSION

Conducting an ethical pilot study in the pilot phase of the main study was, in our view, an effective way of identifying ethical issues likely to arise during the conduct of the main study and provided an evidence base for designing ways of dealing with the issues. Our study had limitations: the small number of participants meant that saturation (the point where no new themes emerge from the data) was probably not reached and well-educated female participants were over-represented in the sample, despite diligent attempts to ensure a spread on these variables. The results are not intended to be generalisable. Indeed, our argument is that an ethical pilot study should be conducted in every major study on genetic testing, precisely because different study populations may have different levels of prior knowledge and different concerns.

As an approach to ensuring the ethical conduct of genetic research, or indeed any research likely to be ethically contentious or sensitive, this is far superior to having researchers and research ethics committees speculate on what may be the concerns of participants and how these can best be dealt with. It provides some evidence on which to base decisions about the specific practical steps that are needed in a particular research context to fulfil the general ethical requirements of ensuring free and informed consent and minimising risk of harm of all kinds to participants. In this sense, we suggest that conducting ethical pilot studies as a matter of routine is a more effective way of ensuring the ethical conduct of genetic research than simply attempting to follow guidelines. This can be confirmed by conducting ethical follow-up studies to investigate the experience of

participants on the research, and to what extent they believed they had a good understanding of what would happen. Guidelines, even those specifically targeted at genetic research, are necessarily general; the ethical pilot study and follow-up provides specific useful guidance.


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## REFERENCES


1 **The American Society of Human Genetics**. Statement on informed consent for genetic research. *Am J Hum Genet* 1996;**59**:471–4.
2 **Beskow LM**, Burke W, Merz JF, *et al*. Informed consent for population-based research involving genetics. *JAMA* 2001;**286**:2315–21.
3 **Weir RF**, Horton JR. Genetic research, adolescents and informed consent. *Theor Med* 1995;**16**:347–73.
4 **Reilly PR**, Boshar MF, Holzman SH. Ethical issues in genetic research; disclosure and informed consent. *Nat Genet* 1997;**15**:16–20.
5 **Ross LF**. Disclosing misattributed paternity. *Bioethics* 1996;**10**:114–30.
6 **NHMRC**. *National statement on ethical conduct in research involving humans*. London: NHMRC, 1999, http://www7.health.gov.au/nhmrc/publications/humans/preamble.htm (accessed 22 Jun 2005).
7 **Tri-Council Policy Statement**. *Ethical conduct for research involving humans*, MRCRM, 1998. http://pre.ethics.gc.ca/english/policystatement/policystatement.cfm (accessed 24 Jul 2006).
8 **Grundfast KM**, Siparsky N, Chuong D. Genetics and molecular biology of deafness. Update. *Ontolaryngol Clin North Am* 2000;**33**:1367–94.
9 **Willems PJ**. Genetic causes of hearing loss. *New Engl J Med* 2000;**342**:1101–9.
10 **Lidz CW**, Appelbaum PS, Grisso T, *et al*. Therapeutic misconception and the appreciation of risks in clinical trials. *Soc Sci Med* 2004;**58**:1689–97.
11 **Appelbaum PS**, Lidz CW, Grisso T. Therapeutic misconception in clinical research: frequency and risk factors. *Rev Hum Subj Res* 2004;**26**:1–8.
12 **Vitiello B**, Aman MG, Scahill L, *et al*. Research knowledge among parents of children participating in a randomized clinical trial. *J Am Acad Child Adolesc Psychiatry* 2005;**44**:145–9.
13 **Weinfurt KP**, Sulmasy DP, Schulman KA, *et al*. Patient expectations of benefit from phase I clinical trials: linguistic considerations in diagnosing a therapeutic misconception. *Theor Med Bioethics* 2003;**24**:329–44.